Conversion of Human Fibroblasts into Monocyte-Like Progenitor Cells.

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Authors: Julian Pulecio, Emmanuel Nivet, Ignacio Sancho-Martinez, Marianna Vitaloni, Guillermo Guenechea, Yun Xia, Leo Kurian, Ilir Dubova, Juan Bueren, Leopoldo Laricchia-Robbio, Juan Carlos Izpisua Belmonte

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Public Summary:
Reprogramming technologies have emerged as a promising approach for future regenerative medicine. Here we report on the establishment of a novel methodology allowing for the conversion of human fibroblasts into Hematopoietic Progenitor-like Cells (HPC) with macrophage differentiation potential. SOX2 overexpression in human fibroblasts, a gene found to be upregulated during hematopoietic reconstitution in mice, induced the rapid appearance of CD34+ cells with a concomitant upregulation of mesoderm-related markers. Profiling of Cord Blood hematopoietic progenitor cell populations identified miR-125b as a factor facilitating commitment of SOX2-generated CD34+ cells to immature hematopoietic-like progenitor cells with grafting potential. Further differentiation towards the monocytic lineage resulted in the appearance of CD14+ cells with functional phagocytic capacity. In vivo transplantation of SOX2/miR-125b-generated CD34+ cells facilitated the maturation of the engrafted cells towards CD45+ cells and ultimately the monocytic/macrophage lineage. Altogether, our results indicate that strategies combining lineage conversion and further lineage specification by in vivo or in vitro approaches could help to circumvent long-standing obstacles for the reprogramming of human cells into hematopoietic cells with clinical potential. Stem Cells 2014.

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